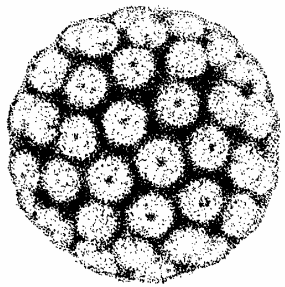
Question 1

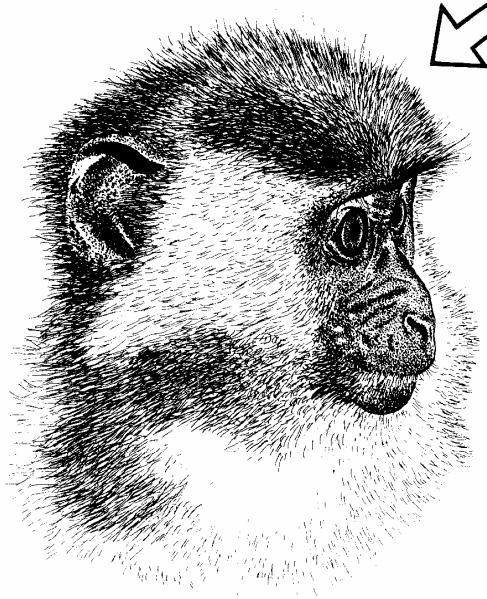
- Do we need to implement more general screening assays for oncogenic viruses?
- If so which viruses? e.g., Polyomaviruses, herpesviruses and retroviruses.
- If so what type of assays?
  - PERT retrovirus
  - RDA, redundant PCR
  - In vivo assays newborn mice, rats, hamsters

LYMPHOTROPIC PAPOVAVIRUS



LPV is a polyomavirus

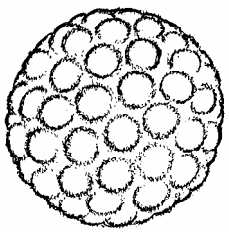
Lymphotropic Papovavirus



African Green Monkey
50% seropositive

- Isolated from African Green Monkey lymphoid cells
- Replicates in B-cells including human B-cells
- Can transform hamster cells
- Related viruses may be present in the human population
  30% of deaths have Ab to LPV, not cross reactive
  with human polyomaviruses
- Related virus recently detected by PCR in Macaques

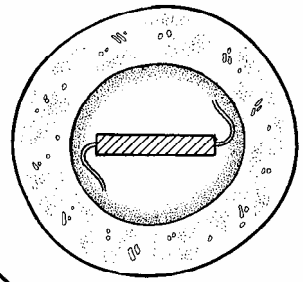
SYRIAN HAMSTER POLYOMA VIRUS



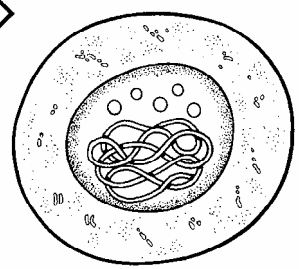
HaPV middle T
containing polyomavirus

Colony outbreaks of
lymphoma or
epeithelioma reported

Hap strain
hamster

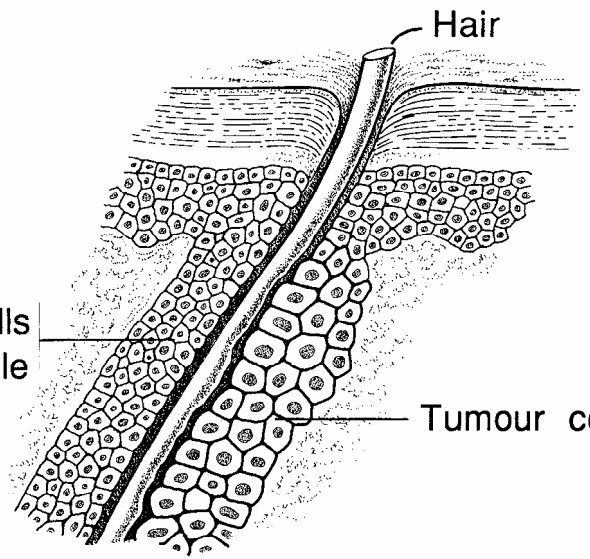


Lymphoma with single
integrated HaPV genome
deleted late region



Lymphoma with
episomal virus
deleted in late region

23 strain
hamster



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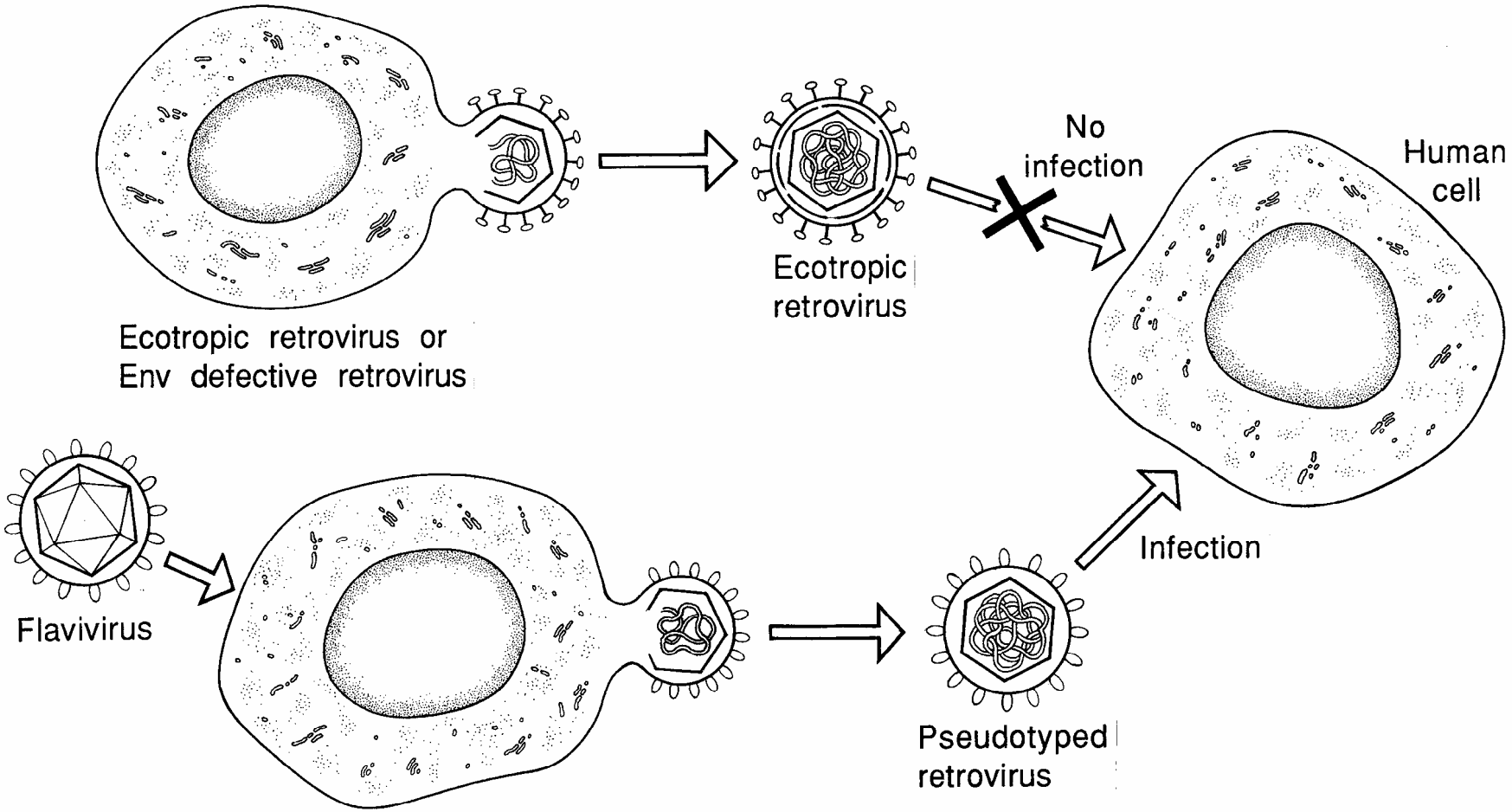
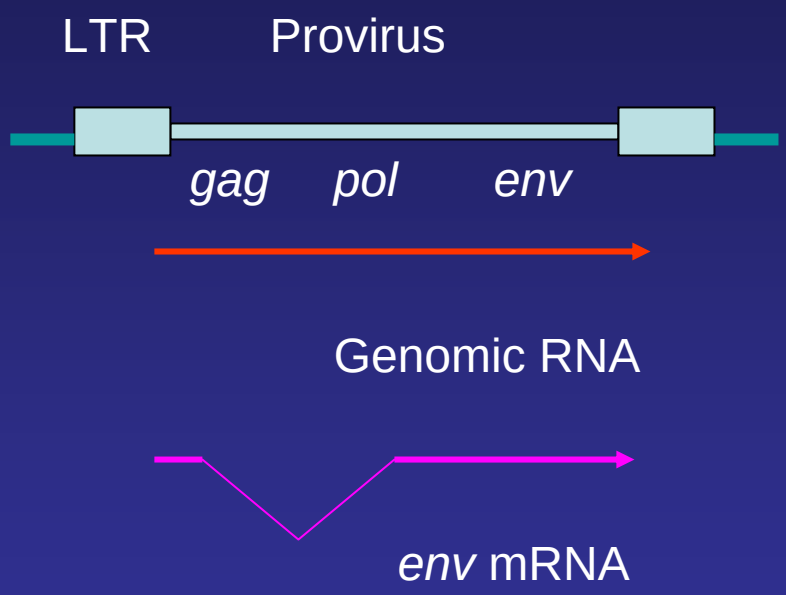
Question 2

- Should we look for novel viral interactions
  - e.g pseudotype formation) in novel cell substrates?
  - Potential complementation of defective oncogenic viruss by vaccine viruses.

FLAVIVIRUSES AND ALPHA VIRUSES MAY PSEUDOTYPE DEFECTIVE OR ECOTROPIC RETROVIRUS



Vero Cells Contain Two main Family of Proviruses



- Mac family
- BaEV family
- Neither expressed as complete virus particles but unknown if env expressed.

Question 2

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  - e.g pseudotype formation) in novel cell substrates?
  - Potential complementation of defective oncogenic viruss by vaccine viruses.

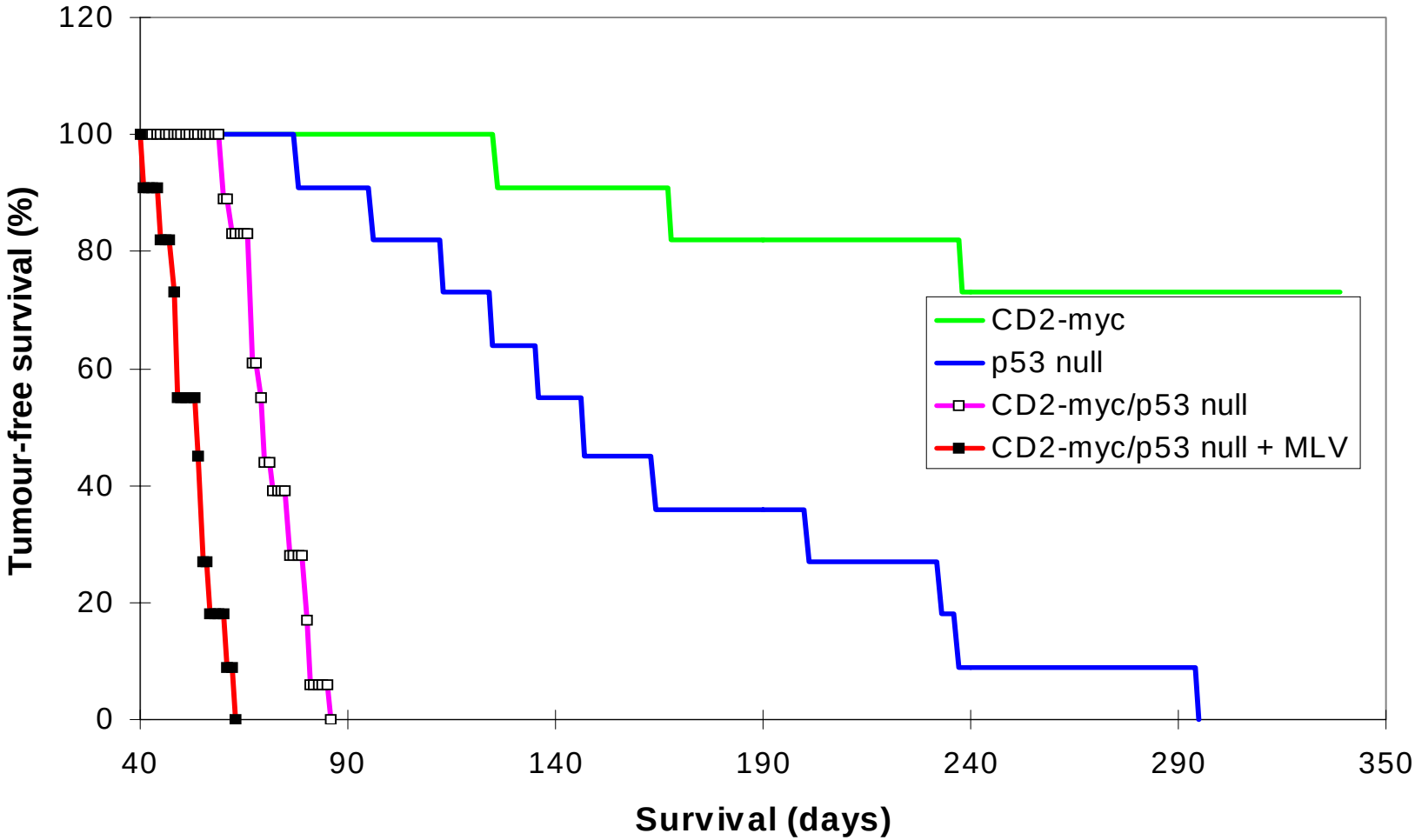
Question 3

- Do the observations of SV40 sequences in human tumours have implications for the continued use of primary cells?

Question 4

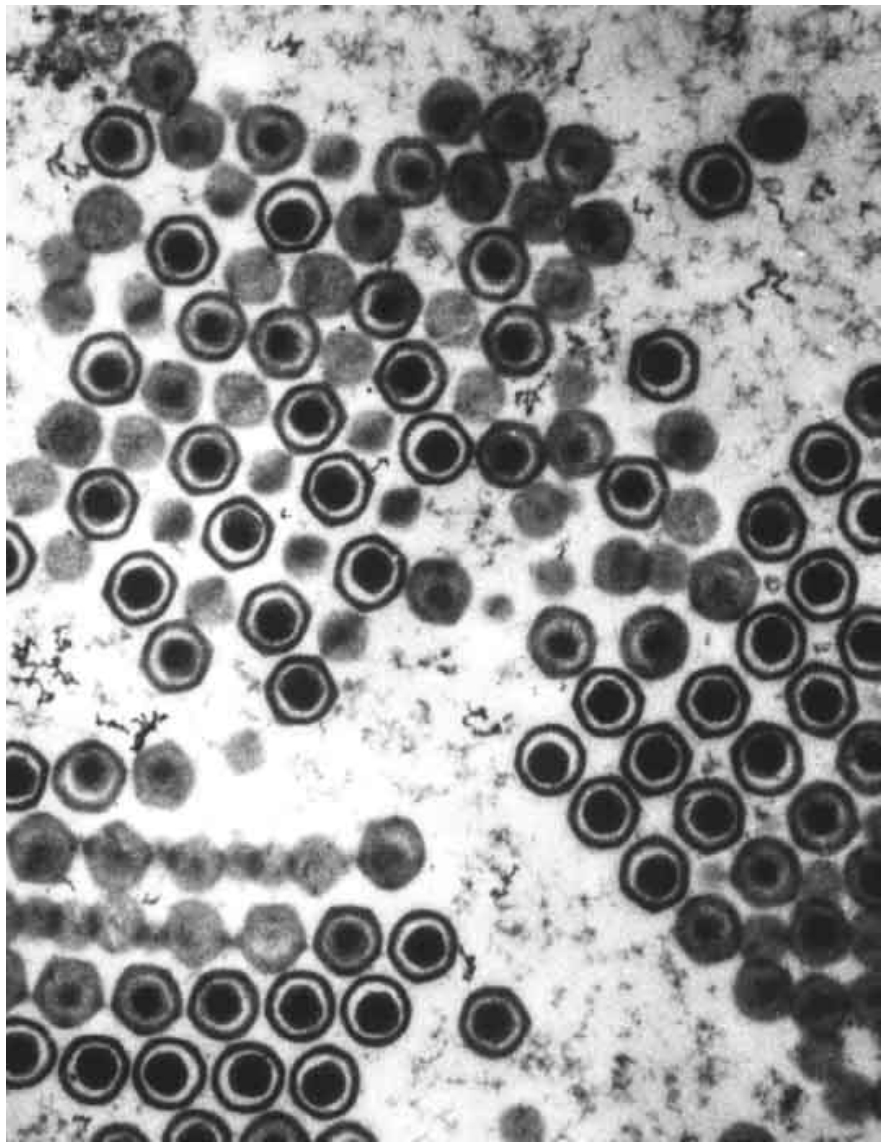
- Is the potential for infectious virus to be transmitted in DNA form relevant to the safety of vaccines ?

Tumour-free Survival of MLV-infected CD2-myc/p53 Null Mice



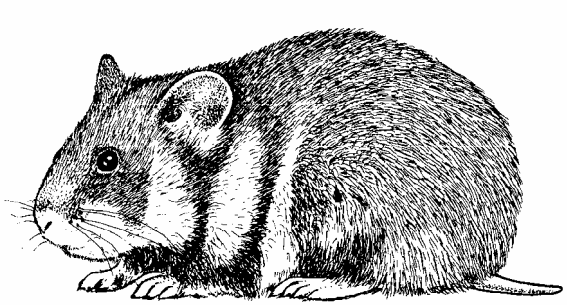
University of Glasgow, Molecular Oncology Group (Blyth *et al*)

Expect the Unexpected

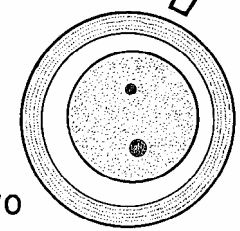


100 nm

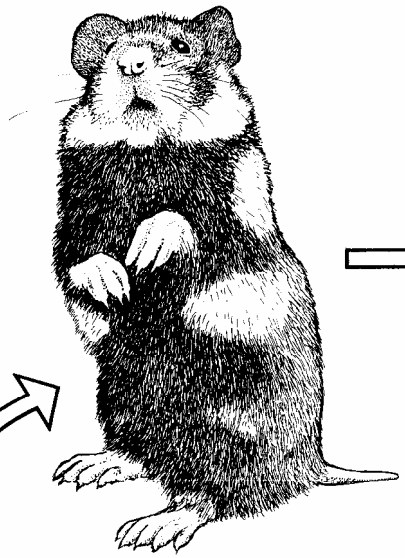
PRIMARY HAMSTER CELLS FROM SPF COLONY



Original strain used for JEV vaccine production

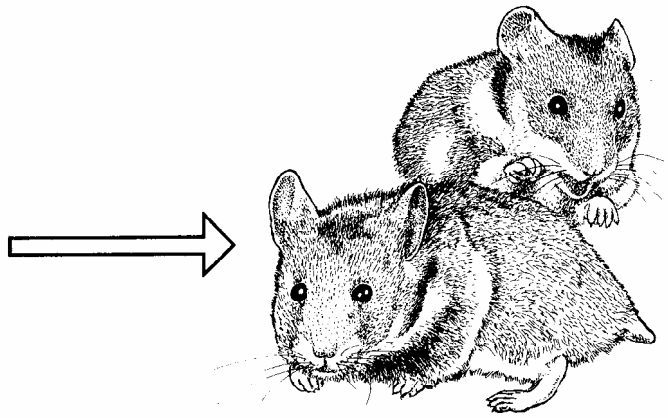


Embryo transfer



SPF recipient female screened by

- HAP

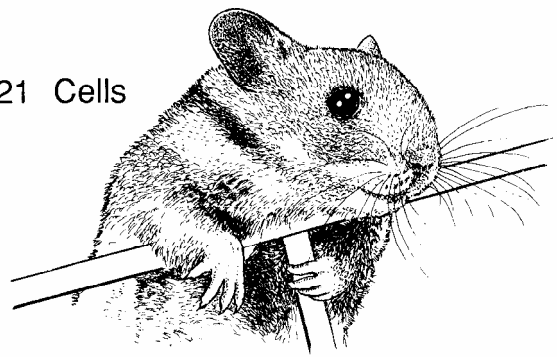


New founders screened by

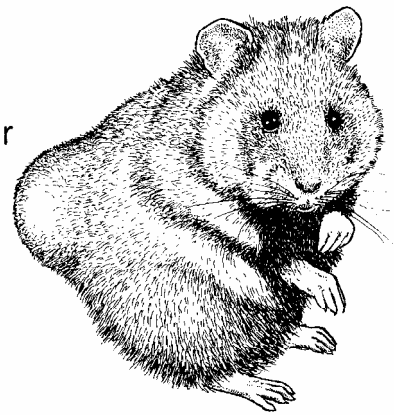
- HAP
- PCR for hamster polyomavirus before and after immunosuppression
- Evaluate kidney cells for HaLV I induction

BHK-21 CELLS READILY FORM TUMOURS BUT THIS IS SUPPRESSED BY CONCURRENT VIRUS INFECTION

5-100
BHK-21 Cells

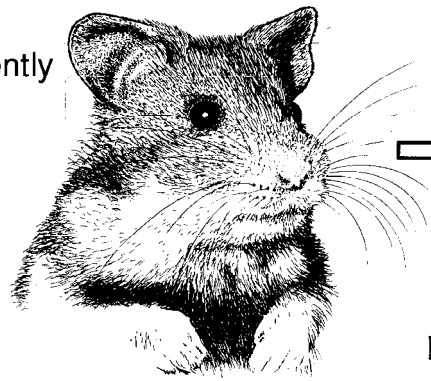


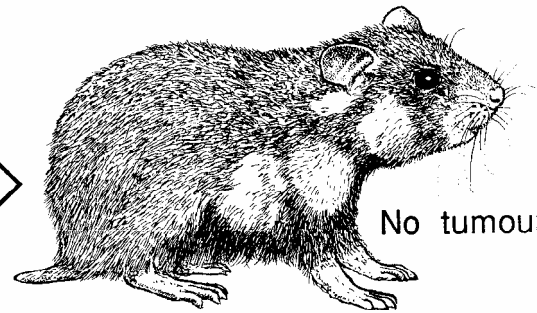
Tumour



2×10^7 cells persistently infected with

- measles
- mumps
- VSV
- influenza

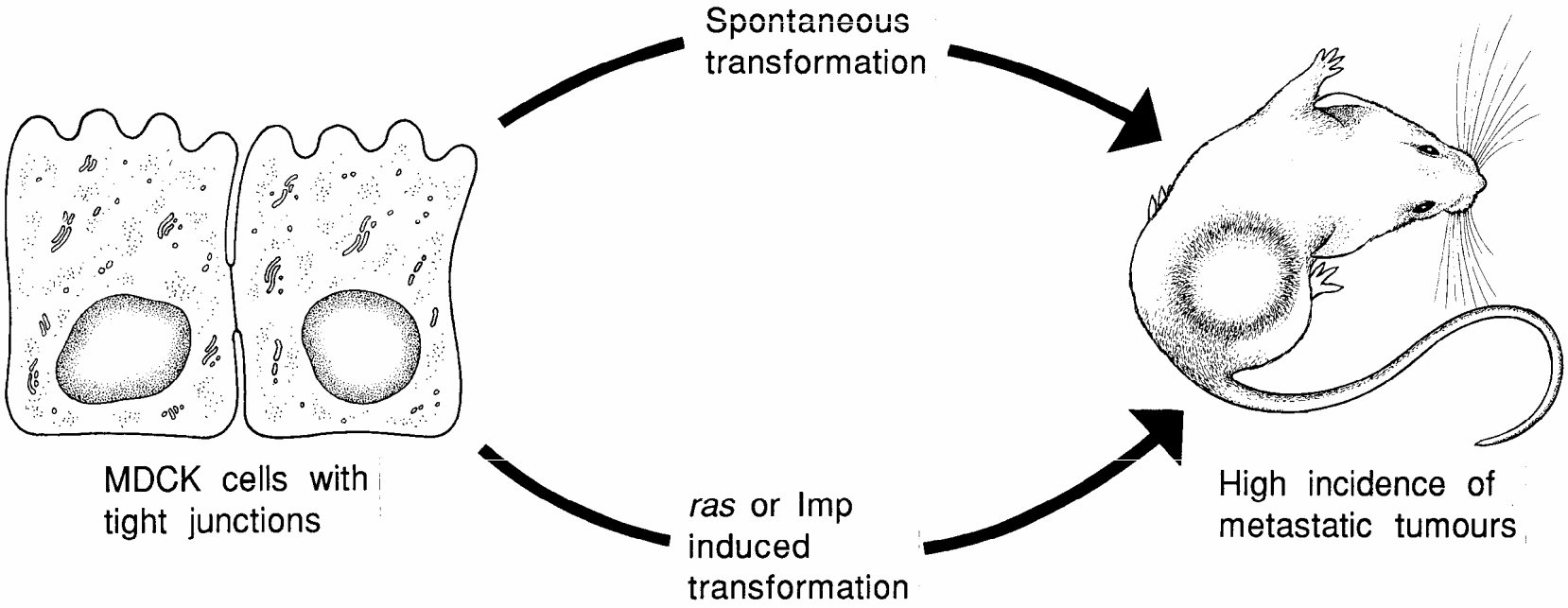




No tumours

Regan & Petricciani (1987) Dev Biol Stand **68**, 19-25
Minato *et al* (1979) J Exp Med **149**, 1117

MDCK CELLS ARE READILY TRANSFORMED BY THE *ras* COMPLEMENTATION GROUP OF ONCOGENES



MDCK cells probably have multiple transforming "genetic hits" including in the *myc* complementation group